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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,535	05/31/2000	Jean-Christophe Francis Audonnet	454313-2335.1	6015

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EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
1632	16

DATE MAILED: 12/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/586,535	AUDONNET ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13,15-26,28-35,37 and 39-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13,15-26,28-35,37 and 39-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment and Remarks filed on September 10, 2002 have been entered as Paper #15. Claims 18, 20-26, 39 have been amended, claims 14, 27, 36, and 38 have been canceled, claims 40-68 are newly submitted. Claims 12, 13, 15-26, 28-35, 37, and 39-68 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and arguments will not be reiterated.

Claim Objections

Claims 67 and 68 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 67 and 68 depend from two composition claims, and are drawn to routes of administering a composition, which would further limit a method claim but not a composition claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 40 and 41 are objected to because the claims are grammatically incorrect, redundant, and confusing. A period and the word "and" should follow "PCV-1" in line 3 of both claims, and the phrase that defines plasmid in line 5 is redundant.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-64, 67, and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly submitted claims 40 and 41 are vague and indefinite because they recite, "a method for enhancing the immunogenicity of a polypeptide...comprising administering the at least one plasmid as a complex with an adjuvant...". The method step may enhance a host immune response to the polypeptide, but not the immunogenicity of the polypeptide itself, the chemical structure and the immunogenicity of the polypeptide have not changed after being complexed with the recited formula.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 12, 15-26, 28-35, 37, and 39 has been modified under 35 U.S.C. 103(a) as being unpatentable over *Poet et al* (US 6,217,883), in view of *Nabel et al* (US 5,910,488), and the rejection applies to the amended and newly submitted claims 40, and 42-68, for reasons of record in paper #14 and following.

New claims are drawn to methods of using the immunogenic composition defined by previous composition claims, and particularly via intramuscular and intradermal routes of delivery. Poet et al teach using such routes of delivery (column 9, lines 56-57).

In paper #15, applicants argue that Nabel do not teach or suggest the use of a lipid complexed with DNA plasmids as an adjuvant to enhance immunogenicity.

The argument has been fully considered but they are not persuasive for reasons of record in paper #14 and following.

With regards to interrelations of the DNA and cationic lipid, as cited in paper #14 and reiterated here, *Poet et al* teach that the DNA vaccines can be incorporated in liposomes to enhance *in vivo* transfection (column 8, lines 13-15). *Navel et al* clearly teach the lipid of interest (DRIME complexed plasmid in gene delivery, wherein the hydroxyl radical is bound to the R^4 carbon atoms in the structure of DMRIE, see enclosed structural display for DMRIE), and its use in DNA vaccination, Navel patent provides plasmids for gene transfer in vivo (tables 1 & 2), and teaches, "ACCORDING TO ONE EMBODIMENT OF THE INVENTION, THE VECTORS PROVIDED HEREIN ARE COMPLEXED WITH CATIONIC LIPOSOMES OR LIPID VESICLES" (column 15, lines 32-46). Apparently, both cited patents teach cationic lipid complexed with DNA plasmid.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Poet et al*, by simply including one of the cationic lipid adjuvant, such as DMRIE alone or coupled with DOPE as taught by *Nabel et al,* with a reasonable expectation of success. One of skilled in the art would have been motivated to do so, because these adjuvants could enhance the

efficiency in DNA transfection *in vivo,* thus, achieve an enhanced vaccine effect. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 13, 18-26, 37, 39, 41, 45-53, 65 and 66 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Poet et al* (US 6,217,883) as evidenced by *Meehan et al* (J Gen Virol 1998;79:2171-79), in view of *Mathiowitz et al* (US 6,475,779).

Poet et al teach an immunogenic preparation (vaccine) comprising a nucleic acid encoding a porcine circovirus, particularly the ORF region of the PCV-I (column 5, lines 40-62), and using the DNA vaccine for inducing an immunological response comprising administering to a porcine said vaccine (Sections starting from line 55 of column 3, SEQ ID Nos: 1, 2, 20-32), which nucleic acids are preferably constructed in a plasmid (lines 56-61). *Poet et al* further teach that in addition to the PCV coding region, the construct could include cytokine-coding region, such as GM-CSF or IL-12 (column 4, lines 61-67) to bring out the specific level of immune response needed to protect the animal from the targeted disease. According to *Meehan et al* (abstract, right column in page 2176), the disclosed sequences (SEQ ID Nos: 1 & 2) of *Poet et al* are correspondent to ORF1 of PCV-I. *Poet et al* go on to teach that the DNA vaccines can be administered in combination with one or more DNA vaccine preparations for viral diseases such as porcine parvovirus (column 7, lines 57-67); and can be incorporated in liposomes to enhance *in vivo* transfection (column 8, lines 1-16, particularly line 14). *Poet et al* teach

using intramuscular and intradermal routes of delivery (column 9, lines 56-57). *Poet et al* do not teach the adjuvant formulation comprising a carbomer.

The specification teaches the term carbomer embraces compounds such as the polymers of acrylic or methacrylic acid crosslinked with polyalkenyl ethers of sugars or of polyalcohols.

Mathiowitz et al teach a method for obtaining efficient introduction of exogenous genes into a patient comprising encapsulating or dispersing a biocompatible polymeric matrix with genetic vectors (abstract). The polymeric matrix includes polymers of acrylic and methacrylic esters (column 4, lines 14 and 15), and co-polymers of polyalkylene (column 4, line 7). The vectors to be delivered include plasmid vectors (working examples). *Mathiowitz et al* teach that in such a matrix form, the transgene is able to diffuse out of the matrix over an extended period of time and increase the effectiveness of gene transfer (column 3, lines 8-32)

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Poet et al*, by simply including an adjuvant compound comprising a carbomer in the formulation of the adjuvant and the PCV vaccine preparation with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
December 13, 2002

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SUPERVISORY PATENT EXAMINER
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